

### **AMENDMENTS TO THE CLAIMS**

The below listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method for detecting a neoplasia in a biologic sample, the method comprising quantifying the promoter methylation of at least two promoters in the sample, wherein one of the promoters is *pi-class glutathione S-transferase (GSTP1)* and the second promoter is selected from the group consisting of *O<sup>6</sup>-methylguanine DNA methyltransferase (MGMT)*, *p14/ARF*, *p16/INK4a*, *RAS-associated domain family 1A (RASSF1A)*, *adenomatous polyposis coli (APC)*, *tissue inhibitor of metalloproteinase-3 (TIMP3)*, *S100A2*, *cellular retinoid binding protein 1 (CRBP1)*, and *retinoic acid receptor  $\beta$ 2 (RAR $\beta$ 2)*, wherein an increased quantity of promoter methylation relative to a reference indicates the presence of a neoplasia in the sample.

2. (Original) The method of claim 1, wherein the second promoter is selected from the group consisting of *APC*, *RASSF1A*, *CRBP1*, and *RAR $\beta$ 2*.

3-4. (Canceled)

5. (Original) A method of determining the clinical aggressiveness of a neoplasia in a biologic sample, the method comprising quantifying the level of *GSTP1* or *APC* promoter methylation in the sample, wherein an increased level of promoter methylation relative to a reference indicates an increased clinical aggressiveness of the neoplasia.

6. (Original) A method of determining the stage of a neoplasia in a biologic sample, the method comprising quantifying the level of promoter methylation in the sample of at least one promoter selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, and *RAR $\beta$ 2*, wherein an increased level of promoter methylation in the sample relative to a reference indicates an increased stage of neoplasia.

7. (Currently amended) The method of claim 1~~any one of claim 1-6~~, wherein the neoplasia is prostate cancer.

8-9. (Canceled).

10. (Currently amended) The method of claim 69, wherein the ~~tissue~~ sample is a prostate tissue sample.

11. (Currently amended) The method of claim 68, wherein the ~~patient~~ sample is a biologic fluid selected from the group consisting of serum, plasma, ejaculate, or urine.

12. (Canceled) .

13. (Currently amended) The method of claim 1~~any one of claims 1-6~~, wherein the reference is the level of methylation present at the promoter in a control sample derived from a healthy subject.

14. (Canceled)

15. (Currently amended) The method of claim 1~~any one of claims 1-6~~, wherein the promoter methylation is quantified by quantitative methylation-specific PCR (QMSP).

16. (Currently amended) The method of claim 1544, wherein the level or the frequency of promoter methylation is quantified.

17. (Canceled)

18. (Currently amended) The method of claim 1~~any one of claims 1-6~~, wherein the methylation levels of the *GSTP1* and *APC* promoters are quantified.

19-36. (Canceled)

37. (Original) A method of determining the prognosis of a subject diagnosed as having a neoplasia, the method comprising quantifying the level of promoter methylation in a sample derived from the subject, wherein at least one promoter is selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2*, and wherein an altered level of promoter methylation relative to a reference indicates the prognosis of the subject.

38. (Currently amended) The method of claim 37, wherein the alteration is a decrease or an increase in the level of promoter methylation relative to a reference.

39. (Currently amended) The method of claim 38, wherein the increased or decreased level of promoter methylation indicates a poor prognosis or a good prognosis.

40-43. (Canceled)

44. (Original) A method of monitoring a subject diagnosed as having a neoplasia, the method comprising quantifying the level of promoter methylation in a sample derived from the subject, wherein at least one promoter is selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2*, and wherein an altered level of promoter methylation relative to the level of methylation in a reference indicates an altered severity of neoplasia in the subject.

45. (Currently amended) The method of claim 37 ~~any one of claims 20-44~~, wherein the reference is the level of methylation present in a sample previously obtained from the subject prior to therapy or present in a normal patient sample.

46-50. (Canceled)

51. (Original) The method of claim 44~~50~~, wherein the tissue sample is a prostate tissue sample.

~~52-54.~~ (Original) The method of claim 44 ~~49~~, wherein the patient sample is a biologic fluid selected from the group consisting of serum, plasma, ejaculate, or urine.

52. (Canceled)

53. (Currently Amended) The method of claim 37~~any one of claims 20-52~~, wherein the promoter methylation is quantified by quantitative methylation-specific PCR.

~~54-57.~~ (Canceled)

58. (Original) A method of selecting a treatment for a subject diagnosed as having a neoplasia, the method comprising:

(a) quantifying the level of promoter methylation in a biologic sample from the subject relative to a reference, wherein the level of promoter methylation is indicative of a treatment; and

(b) selecting a treatment.

59. (Currently amended) The method of claim 58~~any one of claims 20-58~~, wherein the neoplasia is prostate cancer.

60. (Original) A method of selecting a treatment for a subject diagnosed as having prostate cancer, the method comprising:

(a) quantifying the level of promoter methylation of a promoter selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2* in a subject sample; and

(b) selecting a treatment for the subject, wherein the treatment is selected from the group consisting of surveillance, surgery, hormone therapy, chemotherapy, and radiotherapy.

61. (Original) A method for determining the methylation profile of a prostate cancer, the method comprising quantifying the level of promoter methylation at two or more promoters selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2* in a biologic sample, wherein the level of promoter methylation relative to a reference determines the methylation profile of the prostatic neoplasia.

62. (Original) A kit for the analysis of promoter methylation, the kit comprising at least one primer capable of distinguishing between methylated and unmethylated promoter sequences, wherein the promoter sequences are selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2*, and directions for using the primer for the analysis of promoter methylation.

63. (Currently amended) ~~A the kit of claim 62, for the analysis of promoter methylation, the kit comprising at least one pair of primers capable of amplifying a promoter sequence selected from the group consisting of *GSTP1*, *APC*, *RASSF1A*, *CRBP1*, and *RARβ2*, wherein at least one of the primers binds selectively to a methylated or unmethylated sequence.~~

64-68. (Canceled)

69. (Original) A microarray comprising at least two nucleic acid molecules, or fragments thereof, bound to a solid support, wherein the two nucleic acid molecules are selected from the group consisting of *GSTP1*, *MGMT*, *p14/ARF*, *p16/INK4a*, *APC*, *RASSF1A*, *TIMP3*, *S100A*, *CRBP1*, and *RARβ2*.

70. (Original) A method for detecting a neoplasia in a biologic sample, the method comprising quantifying the promoter methylation of at least two promoters in the sample by contacting the sample with a microarray of claim 59, wherein one of the promoters is selected from the group consisting of *GSTP1*, *MGMT*, *p14/ARF*, *p16/INK4a*, *APC*, *RASSF1A*, *TIMP3*, *S100A*, *CRBP1*, and *RARβ2*, and wherein an

increased quantity of promoter methylation relative to a reference indicates the presence of a neoplasia in the sample.

71. (Original) A primer having a nucleic acid sequence selected from the group consisting of:

5'- TGG TTT CGA TTT TTT GAT TTC G -3' (SEQ ID NO:1).

5'- TCA AAA TTC TTT TTA CAA CAA CGC C -3' (SEQ ID NO:2),

5'- CTG GGA ATC CAG CTG TCG CCG CCC CGC A -3' (SEQ ID NO:4), 5'-  
GCG CAT CAT AGC CAT CAG CAA CAA A -3' (SEQ ID NO:5),

5'-CGA GAA CGC GAG CGA TTC-3' (SEQ ID NO:7),

5'-CAA ACT TAC TCG ACC AAT CCA ACC-3' (SEQ ID NO:8),

5'-TGG TGA TGG AGG AGG TTT AGT AAG T-3' (SEQ ID NO:10)

5'- AAC CAA TAA AAC CTA CTC CTC CCT TAA-3'(SEQ ID NO:11).

72. (Original) A probe having a nucleic acid sequence selected from the group consisting of:

5'- CGA CCG AAC GCG ATA ACT TAC TCC -3'-TAMRA (SEQ ID NO:3), 5'-  
GAC CCG AAA ATA AAC GCC CTC CGA AAA CA -3' (SEQ ID NO:6),

5'-TCG GAA CGT ATT CGG AAG GTT TTT TGT AAG TAT TT-3' (SEQ ID  
NO:9),

5'-ACC ACC ACC CAA CAC ACA ATA ACA AAC ACA-3' (SEQ ID NO:12).

73. (Original) A collection of primer sets, each of said primer sets comprising at least two primers that bind to a promoter selected from the group consisting of *GSTP1*, *MGMT*, *p14/ARF*, *p16/INK4a*, *APC*, *RASSF1A*, *TIMP3*, *S100A*, *CRBP1*, and *RARβ2*, said collection comprising at least two primer sets.